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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/716,344	11/26/1996	ROLF ENGSTAD	CU-1446TJK	5681

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EXAMINER	
PRATS, FRANCISCO CHANDLER	
ART UNIT	**PAPER NUMBER**
1651	13

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/716,344	ENGSTAD ET AL.	
	Examiner	Art Unit	
	Francisco C Prats	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 May 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The amendment filed May 2, 2003, has been received and entered. The text of those sections of Title 35, U.S. Code, not included in this action can be found in a prior office action.

Claims 17-19 have been added.

Claims 1-19 are pending and are examined on the merits.

Information Disclosure Statement

The information disclosure statement (IDS) filed May 2, 2003, fails to comply with 37 CFR 1.97(c) because it lacks a statement as specified in 37 CFR 1.97(e) and because it lacks the fee set forth in 37 CFR 1.17(p). An IDS may be considered after first action on the merits if either the fee is paid or a Rule 1.97(e) statement is supplied. See 37 CFR 1.97(c). Because neither of these actions has been performed, the IDS has been placed in the application file, but the information referred to therein has not been considered.

Claim Rejections - 35 USC § 112

Claims 1-19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably

convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Specifically, the new recitation in the claims ", containing four or less β-1,6-bound glucose units" now requires the glucan molecule recited in the claims to be essentially free of β-1,6-linked chains having four or less β-1,6-bound glucose units. The as-filed specification does not support this new limitation. It is noted that page 4, lines 9-16, of the specification states that the enzyme action results in a molecule "essentially free" of branches of more than 1 glucose unit. The same portion of the specification also goes on to state that enzymatic action removes "most" chains having more than 4 β-1,6-bound glucose units. However, the specification does not state the degree to which cleavage occurs on "chains" containing 2, 3, or 4 glucose units. That is, the fact that "most" of the chains of length greater than 4 glucose units are cleaved from the molecule does not result in a necessary conclusion that essentially all of the chains of 4 glucose units or less are cleaved from the molecule. It is therefore unclear where applicant obtains support for the new language.

Claims 1-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation "essentially free" (claims 1, 7, 8, 9, 13 and 16) is indefinite because it is not clear what percentage of β-1,6-linked chains must be eliminated for a particular glucan to be considered essentially free of such chains.

All of applicant's argument regarding this ground of rejection has been fully considered but is not persuasive of error. While applicant argues that the amendment to the claims clarifies this issue, it is simply unclear what "essentially free" means, even when the term is taken in light of the specification. One of ordinary skill would generally construe the term to mean that no β-1,6-linked chains of 4 or less glucose chains are present. However, the paragraph appearing at page 4, lines 9-16, of the specification, initially states that enzyme action results in a molecule essentially free of β-1,6-linked chains of 4 or less glucose chains, but later states that "most" larger chains are removed. Thus, the paragraph appearing at page 4, lines 9-16, of the specification provides two contradictory meanings for "essentially free," the first being

the expected meaning, and the second being that most of the undesired side chains are removed. It is simply unclear on the record how many β-1,6-linked chains of 4 or less glucose chains are present on the claimed product. The rejection must therefore be maintained.

Claim Rejections - 35 USC § 102

Claims 1, 4, 5, 7, 9, 10, 13, 14 and 16-19 are rejected under 35 U.S.C. 102(b) as being anticipated by Shiota et al (J. Biochem. 98:1301-1307 (1985)).

Shiota et al disclose a process wherein the claim-designated polysaccharide, *Saccharomyces cerevisiae* β-glucan, is hydrolyzed with the claim-designated enzyme. *See* p. 1303. ("Enzymatic hydrolysis of the skeletal glucan was performed with . . . *Neurospora crassa* endo-(β-1-6)-glucanase. The sample (about 100 mg) was incubated with . . . the endo-(β-1-6)-glucanase (2.8 U) in 2 ml of sodium acetate buffer (0.01 M, pH 5.0) at 35 C for 24 h.").

It is noted that the claims have been amended to require the glucan to be in insoluble particulate form, and that the glucans are essentially free of β-1,6-linked chains of 4 or less glucose chains. As an aside note that applicant's marked-up copy of claims 1 and 7 failed to indicate that the term

"particulate" was newly inserted at line 2 of each of those claims. Regardless, the limitation requiring insoluble particles is considered to be met by Shiota based on the fact that the glucan prepared by Shiota is the insoluble fraction obtained by alkali and acid extraction. See page 1302, right hand column, paragraph entitled "*Preparation of Cell Wall Skeletal Glucan.*" Note specifically that this is a virtually identical process by which the glucan starting material is prepared in Example 1 of applicant's specification.

Similarly, Shiota meets the new limitation requiring the glucans to be essentially free of β-1,6-linked chains of 4 or less glucose chains because Shiota contacts the identical material as claimed with an enzyme having an identical catalytic activity. By subjecting the same material as claimed to the same conditions, the result must necessarily be the same. The laws of chemistry require it. Thus Shiota anticipates the claimed processes and products.

All of applicant's argument regarding this ground of rejection has been fully considered but is not persuasive of error. Applicant initially argues that the glucanase used by Shiota is from a different microorganism than the claimed glucanase. However, it is respectfully pointed out that none of the claims in this ground of rejection recite anything about the

source microorganism for the enzyme. Thus, applicant is arguing about a limitation not present in the claims.

Also, with respect to Shiota's use of acetic acid as a solubilizing agent asserted by applicant, note specifically that applicant's claims recite the process in open "comprising" language, which encompasses the use of reagents and steps not specifically recited in the claims. Moreover, to the extent that Shiota prepares the glucan starting material using acetic acid extraction, note specifically that applicant's own method of preparing the glucan starting material uses acetic acid extraction, directly contrary to applicant's argument. See specification at page 6, lines 18 and 19. ("The insoluble residue remaining was then adjusted to pH 4.5 with acetic acid.")

Further still, applicant's assertion that the claimed glucan product is different from Shiota's glucan product is not based on any fact in evidence. Rather, applicant states that the products are different, without offering any evidentiary support whatsoever for that statement. Shiota contacts a starting material identical to the claimed starting material with an enzyme having a catalytic activity identical to the claimed enzyme. The inevitable result is that the resulting product will be the same. Because applicant has failed to

provide any evidence that the products are different, the rejection must be maintained.

Claim Rejections - 35 USC § 103

Claims 1-3 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shiota et al (J. Biochem. 98:1301-1307 (1985)) in view of de la Cruz et al (Arch. Microbiol. 159:316-322 (1993)).

Claims 2 and 3 limit the β-1,6-glucanase of claim 1 to an enzyme obtained from *Trichoderma harzianum*. As discussed immediately above, Shiota anticipates claim 1. However, the β-1,6-glucanase used by Shiota is from a different microorganism than the claimed β-1,6-glucanase. Despite this difference, the artisan of ordinary skill at the time of applicant's invention would have recognized and reasonably expected that any -1,6-glucanase, including the β-1,6-glucanase disclosed by de la Cruz, could have been used equivalently to the β-1,6-glucanase used in the Shiota process. Thus, because the process recited in claims 2 and 3 differs from Shiota only in the use of a known equivalent β-1,6-glucanase enzyme, the process recited in claims 2 and 3 would have been obvious at the time of applicant's invention.

All of applicant's argument regarding this ground of rejection has been fully considered but is not persuasive of error. Applicant asserts that the claimed combination of references cannot render the claimed subject matter obvious because the claimed product is different from that disclosed by Shiota et al. However, as discussed above, applicant has provided no evidence in support of this assertion. On the current record it is clear that the same starting material as claimed, yeast glucan, is contacted with an enzyme having the same catalytic activity as claimed, endo-β-1,6-glucanase activity. Thus, if there is a difference between Shiota's product and the claimed product, it is due to some unclaimed aspect of the invention. Moreover, because one of ordinary skill would have considered enzymes having endo-β-1,6-glucanase activity to be interchangeably equivalent, regardless of source microorganism, the artisan of ordinary skill would have considered obvious the claimed substitution of de la Cruz's enzyme for Shiota's enzyme. That is, in view of Shiota's disclosure of the requirement for endo-β-1,6-glucanase activity, the artisan of ordinary skill would have considered the use of such an enzyme obvious, regardless of source microorganism. The rejection must be maintained.

Claims 1, 6 and 13-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shiota et al (J. Biochem. 98:1301-1307 (1985)) in view of Jamas (U.S. Pat. 5,028,703).

Claims 6 and 15 limit the processes of claims 1 and 13 to processes wherein specific extraction steps are performed. As discussed above, Shiota anticipates claims 1, 13 and 14. However, Shiota does not disclose processes wherein the exact process steps recited in claims 6 and 15 are performed. Despite this difference, Jamas discloses that, prior to acid or enzymatic treatment, glucan derived from *Saccharomyces cerevisiae* can be extracted from yeast using a variety of extraction techniques under a variety of conditions, including those employed in the process recited in claims 6 and 15. *See e.g.* Jamas at col. 6, lines 3-6. ("The digested glucan particles can be, if necessary, subjected to further washings and extraction to reduce the protein and contaminant level to the preferred amounts hereinbefore indicated.") Moreover, the claimed repetition of extraction steps is disclosed by Shiota, which discloses numerous repetitions of the extraction steps.

Thus, while the exact sequence of process steps recited in claims 6 and 15 are not disclosed by either Shiota or Jamas, both of the references disclose that the claimed steps were conventional in the art at the time of applicant's invention.

Thus, the artisan of ordinary skill at the time of applicant's invention would have deemed the process recited in claims 6 and 15 obvious over the cited references, the claimed process being an optimization of the processes disclosed by Shiota and Jamas, using conventional extraction steps disclosed by those references.

All of applicant's argument regarding this ground of rejection has been fully considered but is not persuasive of error. Applicant again asserts that the claimed combination of references cannot render the claimed subject matter obvious because the claimed product is different from that disclosed by Shiota et al. However, as discussed above, applicant has provided no evidence in support of this assertion. On the current record it is clear that the same starting material as claimed, yeast glucan, is contacted with an enzyme having the same catalytic activity as claimed, endo-β-1,6-glucanase activity. Thus, if there is a difference between Shiota's product and the claimed product, it is due to some unclaimed aspect of the invention. The rejection must therefore be maintained.

Claims 10 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shiota et al (J. Biochem. 98:1301-1307

(1985)) in view of Jamas (U.S. Pat. 5,028,703), and in further view of Matsueda et al (GB 2 076 418).

Claim 11 limits the process of claim 10 to one in which formic acid is employed as the acid solubilizing agent. As discussed above, Shiota anticipates claim 10. However, Shiota does not disclose processes wherein formic acid is employed as the acid solubilizing agent. Rather, Shiota employs acetic acid as the solubilizing agent. Despite this difference, Jamas, which also discloses the use of acetic acid as a glucan solubilizing agent, also discloses that other acids may be employed as solubilizing agents. *See* Jamas at col. 6, line 67, through col. 7, line 3. ("Acetic acid is preferred, due to its mild acidity, ease of handling, low toxicity, low cost and availability, but other acids may be used. Generally these acids should be mild enough to limit hydrolysis of the β(1-3) linkages.") Further still, Matsueda discloses that formic acid can be used as a pre-enzymatic hydrolysis solubilizing agent for an anti-tumor glucan having a β-1,3 glucan backbone and β-1,6 branch structures.

Thus, the artisan of ordinary skill at the time of applicant's invention would have deemed obvious the substitution of the formic acid of Matsueda for the acetic acid used in the Shiota process. The artisan of ordinary skill would have

recognized from the Jamas disclosure that acids mild enough to preserve the β-1,3 glucan backbone could have been used equivalently to the acetic acid used in the Shiota process, and would further have recognized from the Matsueda disclosure that formic acid is such an acid. Thus, the artisan of ordinary skill at the time of applicant's invention would have considered the use of formic acid recited in claim 11 to have been the substitution of one art-recognized equivalent for another, and therefore obvious under § 103.

All of applicant's argument regarding this ground of rejection has been fully considered but is not persuasive of error. While applicant urges that the claimed enzymatic treatment does not solubilize the yeast glucans, it is respectfully pointed out that Shiota's process also results in an insoluble product. See page 1303, left hand column, disclosing that the enzyme-hydrolyzed "precipitate was washed with water and lyophilized", thus clearly disclosing the recovery of an insoluble product. Thus, the insoluble particulate product recited in claims other than claims 10 and 11 is clearly disclosed by Shiota.

Relevant to claims 10 and 11, notably, the soluble supernatant was also recovered. See page 1303. ("The resulting supernatant was applied to a Bio-Gel P-2 column (1.5 x 150 cm

and eluted with water.") Moreover, the product was recovered after combined treatment with enzyme and a pH 5.0 environment. See page 1303 first paragraph, left column. Claims 10 and 11 do not recite any specific amount of solubilizing agent. Thus claims 10 and 11 encompass the use of acid solubilizing agent in an amount which would result in pH 5.0, as disclosed in Shiota. Lastly, in view of Jamas' and Matsueda's clear disclosure of the desirability of solubilizing glucan with formic acid, the artisan of ordinary skill clearly would have been motivated to have used formic acid to have solubilized the glucan of Shiota. In sum, while applicant argues a difference between the claims and the prior art, the claims are sufficiently broad so as to encompass processes suggested by the prior art. The rejection must therefore be maintained.

Claim Rejections - 35 USC § 102/103

Claims 8 and 12 are rejected under 35 U.S.C. § 102(b) as anticipated by or, in the alternative, under 35 U.S.C. § 103 as obvious over Shiota et al (J. Biochem. 98:1301-1307 (1985)).

Shiota et al disclose a glucan product which appears to be identical to the presently claimed glucan product because the product results from contacting the claimed starting material, *Saccharomyces cerevisiae* glucan, with the claimed enzyme, β-1,6

glucanase. Consequently, the claimed product appears to be anticipated by the reference.

While it appears that the prior art product and the claimed product must necessarily be identical, it is noted that the prior art and claimed products are prepared by processes which differ somewhat in their initial extraction steps. However, even if the reference glucan and the claimed glucan are not one and the same and there is, in fact, no anticipation, the reference glucan would, nevertheless, have rendered the claimed glucan obvious to one of ordinary skill in the art at the time the claimed invention was made in view of the clearly close relationship between the products as evidenced by the fact that they are prepared from the same starting material, and are therefore structurally very closely related compounds.

Thus the claimed invention as a whole was clearly *prima facie* obvious especially in the absence of sufficient, clear, and convincing evidence to the contrary.

Regarding propriety of an alternative rejection, note that MPEP § 706.3(e) states that:

> "[w]hen the prior art discloses a product which reasonably appears to be either identical with or only slightly different than a product claimed in a product-by-process claim, a rejection based alternatively on either section 35 U.S.C. 102 or 35 U.S.C. 103 of the statute is appropriate. As a practical matter, the Patent and Trademark Office is not equipped to manufacture

> products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith. A lesser burden of proof is required to make out a case of prima facie obviousness for product-by-process claims because of their peculiar nature than when a product is claimed in the conventional fashion. *In re Brown*, 59 CCPA 1063, 173 USPQ 685 (1972); *In re Fessmann*, 180 USPQ 324 (CCPA1974)."

All of applicant's argument regarding this ground of rejection has been fully considered but is not persuasive of error. As discussed above, applicant has not supported the assertion that the product of Shiota is different than the claimed product by any evidence of record. It is again pointed out that on the current record it is clear that Shiota contacts a starting material identical to the claimed starting material with an enzyme having a catalytic activity identical to the claimed enzyme. The inevitable result is that the resulting product will be the same. If there is some difference between the products, the difference must be due to some unclaimed aspect of the invention. The rejection must therefore be maintained

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is

reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Francisco C Prats whose telephone number is 703-308-3665. The examiner can normally be reached on Monday through Friday, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G Wityshyn can be reached on 703-308-4743. The fax phone numbers for the organization where this application or proceeding is assigned

are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Francisco C Prats
Primary Examiner
Art Unit 1651

FCP
July 10, 2003